REMARKS

A. Status of the claims

Claims 1-36, 38-47 and 52 are canceled, claims 37, 48 and 53 have been amended and new claims 54-56 have been added. Thus, claims 37, 48-51 and 53-56 are currently pending and under examination. The amendments to claims 37 and 53 incorporate structural aspects of claim 41. Likewise, new independent claims 54-56 are based on claims 37 and 41. No new matter has been added. Applicants reserve to right to reintroduce any canceled or amended claims in a future continuation application.

B. Rejections under 35 U.S.C. §103(a) are overcome

The Examiner has rejected claims 37, 39, 41, 48-51 and 53 as assertedly obvious under 35 U.S.C. §103(a) over Starzynska et al. (Eur. J. Gastroenterology & Hepatology 1998, 10(6):479-484) in view of Gnjatic et al. (Eur. J. Immunol. 1995, 25:1638-1642), Theobald et al. (J. Exp. Med. 1997, 185(5): 833-841), Vierboom et al. (J. Exp. Med. 1997,188(5): 695-704), Kobayashi et al. (Cancer Res, 1998, 58: 296-301), Myers et al. et al. (J. Biol. Chem. 1994, 269(12): 9319-9324), Nijman et al. (Eur. J. Immunol. 1993, 23:1215-1219) and WO 98/56919. Applicants traverse the rejection because none of the cited references alone or in combination teacher suggest a vector encoding a HLA CTL peptide epitope of 5T4 antigen. Furthermore, none of the references cited in the rejection disclose the sequences set forth in SEQ ID NOs: 5-17.

In the rejection the Examiner asserts that Myers et al. teaches the nucleotide and amino acid sequence of 5T4. However, Myers et al. does not suggest or disclose that 5T4 is a candidate antigen for immunotherapeutic compositions, and Myers et al. does not suggest that CTL epitopes of 5T4 should be identified or optimized. On the contrary, at the time the instant application was filed, 5T4 would not have been considered a viable candidate antigen for immunotherapy because 5T4 was thought to be expressed on vital organs in subjects as well as on a cancer cells (*see, e.g.,* Table I on page 24 of Stern et al. (WO 89/07947)).

The Examiner further cites Starzynska et al., and states that the reference teaches that 5T4 antigen expression in cancer cells is correlated with poor short-term prognosis for patients having such cancers. Even if this is true, Starzynska et al. merely suggests that 5T4 may be a *prognostic marker* in cancer. Starzynska et al. does not suggest 5T4 as a candidate immunotherapeutic antigen and Starzynska et al. provide no teaching or suggestion or motivation to attempt to identify or optimize CTL epitopes from a prognostic marker. In fact, none of the other references identified by the Examiner and discussed in the Office Action teach or suggest 5T4 as a candidate immunotherapeutic antigen. Absent any suggestion in the art that 5T4 could serve as a candidate immunotherapeutic antigen, the skilled artisan would not have been motivated to make the claimed vectors encoding a HLA CTL peptide epitope according to SEQ ID NOs: 5-17.

The Examiner cites additional secondary references as allegedly teching various aspects of the claimed subject matter. However, none of the references provide any disclosure or suggestion that that 5T4 is a candidate antigen for immunotherapy or any suggestion regarding possible 5T4 CTL epitopes. Thus, the secondary references fail to overcome a deficiency in the rejection. Gnjatic et al., for instance, teaches mapping of potential CTL epitopes in p53 protein for synthesizing peptides, but fails to disclose any information pertinent to 5T4 antigen or possible applications for 5T4. Likewise, Theobald et al. concerns p53 protein and possible uses of p53 T-cell epitopes, but fails to provide any disclosure regarding 5T4 or T-cell epitopes thereof. Vierboom et al. discloses that certain self-antigens may be used as targets for CTL-mediated destruction of tumors, but again fails to suggest 5T4 as a candidate target for such CTL-mediated destruction of tumors amongst the multitude of possible targets.

The Examiner argues that Kobayashi et al. teaches the value of identifying epitopes for design of tumor vaccines for immunotherapy. Again, this reference teaches nothing with regard to 5T4 as a candidate antigen. Nijman et al. discusses the binding motif for a HLA, but Nijman et al. does not discuss 5T4 antigen or any possible uses for this antigen. Finally, WO 98/56919 concerns vaccination regimens which employ a priming vector and a boosting vector, but again this reference has no disclosure concerning 5T4. Thus, no reference identified by the Examiner would provide a motivation or suggestion to a

skilled artisan to identify 5T4 HLA CTL peptide epitopes or generate vectors encoding a HLA CTL peptide epitope of 5T4 antigen, because it was not recognized in the art that 5T4 could be used as a candidate immunotherapeutic antigen or that there would be any value in identifying 5T4 CTL epitopes.

Moreover, literature about 5T4 at the time the instant application was filed would have taught away from the use of 5T4 antigen. In particular, Stern et al. discloses that 5T4 is expressed in a variety of crucial tissues (*see, e.g.,* Table I on page 24 and Table V on pages 33-35) which would have dissuaded the skilled artisan from selecting 5T4 for immunotherapy due to concerns that a 5T4 immune response would induce autoimmune disease involving such organs. Absent hindsight knowledge of the disclosure of the instant application, the skilled artisan would have concluded that 5T4 would *not* have been an acceptable candidate as an immunotherapeutic antigen even if the skilled worker sought to use immunotherapeutic antigens to treat cancer. Likewise, the skilled worker would have been dissuaded from constructing vectors comprising HLA CTL peptide epitope of 5T4 antigen because there would be no apparent use for such vectors in view of the teaching of 5T4 expression on essential tissues. Thus, the knowledge in the prior art would have taught away from the claim recited vectors. In view of the foregoing arguments, Applicants submit that no *prima facie* case for obviousness has been set forth in the removal of this rejection is respectfully requested.

C. Rejections under 35 U.S.C. §112, written description, are overcome

Claims 37, 39, 41,48-51, and 53 have been rejected under 35 U.S.C. § 112, first paragraph as assertedly failing to meet the written description requirement. Applicants continue to traverse the rejections for the reasons the have been previously made of record. Nonetheless, in the interest of expediting prosecution, the Applicants have amended independent claim 37 to recite the limitation of claim 41 (*i.e.,* wherein the peptide epitope is selected from the group consisting of SEQ ID NOs: 5-17). Thus, amended claim 37 recites specific structural elements (SEQ ID NOs: 5-17) that are explicitly provided in the application. Likewise, new claims 54-56 also recite specific structural elements provided as SEQ ID NOs: 15-19 (or SEQ ID NOs: 15-17). In view of this amendment Applicants believe that the instant rejection under 35 U.S.C §112, written description has been overcome.

D. Conclusion

In view of the above amendments and arguments, Applicants believes the pending application is in condition for allowance. The Examiner is invited to call Applicants' representative at the number below with any questions or concerns.

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Respectfully submitted,

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